

**REMARKS**

Claims 1-35, 68, 91, and 112-128 were previously pending in this application. Claims 3, 4, 10, 18, 35 and 112-124 are cancelled herewith. Claims 1, 2, 8, 9, 11, 12, 14, 15, 22, 23, 31-34, 68, 91 and 125-127 are amended. Support for these amendments can be found in originally filed claims 4 and 10 and in the specification at least on page 1 lines 24-25, page 18 line 16, page 20 lines 16-30, and page 21 lines 5-9. The amendments to claims 22 and 23 are not made in response to the instant Office Action and its rejections, and therefore do not narrow the scope of claim 1.

New claims 129 and 130 are added. Support for claim 129 can be found in previously pending claim 125 and in the specification as recited above. Support for claim 130 can be found in previously pending claim 1 and in the specification at least on page 27 line 17.

Claims 1, 2, 5-9, 11-17, 19-34, 68, 91 and 125-130 are pending for examination with claims 1, 68, 91, 125, 126, 129 and 130 being independent claims.

No new matter has been added.

***Objection to the Specification***

Claim 3 is objected to under 37 CFR §1.75(c) as being of improper dependent form. Claim 3 is now cancelled. Accordingly withdrawal of the objection is respectfully requested.

***Rejections under 35 U.S.C. §112***

Claims 33, 34 and 126-128 are rejected under 35 U.S.C. §112 second paragraph as being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33 and 34 are rejected because of insufficient antecedent basis for the limitation “The system of claim ... ”. Claims 33 and 34 are amended to recite “The method of claim ... ”. The claims now find proper antecedent basis in the claims from which each depends.

Claim 34 is further rejected because it contains the trademark “Gene Engine”. Claim 34 is further amended to delete reference to Gene Engine. Applicant is not relinquishing claim scope with this amendment as claim 19 recites “a linear polymer analysis system”. Gene Engine is a linear polymer analysis system.

Claims 126-128 are rejected for omitting essential steps, according to the Examiner. Claim 126 is amended to include the limitation of “thereby labeling the polymer”. Support for this amendment can be found in the specification at least on page 2, line 3-6.

In view of the foregoing amendments, reconsideration and withdrawal of the rejection is respectfully requested.

***Rejections under 35 U.S.C. §102***

*Norton et al., Bioorganic & Medicinal Chemistry 1995*

Claims 1-8, 10-11, 16-18, 24-25, 27-28, 30-31, 91 and 125-128 are rejected under 35 U.S.C. 102(b) as being anticipated by Norton et al. (*Bioorganic & Medicinal Chemistry 1995*).

Norton et al. teaches a site-specific DNA cleavage method in which target DNA sequences are bound and cleaved by PNA-nuclease conjugates. The method is used to determine the binding affinity of PNA to various structural elements in duplex DNA. Cleaved products are then resolved on a gel.

Claims 1, 91 and 126 are amended to recite the limitation that the nucleic acid binding agent is a nucleic acid binding enzyme that binds the polymer without cleavage. New claim 129 recites the same limitation. Support for this limitation can be found in the specification at least on page 20 lines 16-25. Accordingly amended claims 1, 91 and 126 (and their dependents) and new claims 129 and 130 recite methods in which a polymer is analyzed or labeled using conjugates that comprise a nucleic acid binding enzyme that binds the polymer without cleaving it. In addition, claim 126 explicitly recites that the nucleic acid binding enzyme binds and translocates along the target polymer. Cleaving the nucleic acid, as required by the method of Norton et al., would impair the capacity of the enzyme to translocate.

Claim 125 is amended to delete reference to a nucleic acid binding agent that is a nuclease.

The methods of the rejected claims and the new claims are different from those taught by Norton et al. and accordingly Norton et al. does not anticipate these claims.

In view of the foregoing, reconsideration and withdrawal of the rejection is respectfully requested.

*Grigoriev et al. (PNAS 1993)*

Claims 1, 3-9, 13-14, 16-17, 22, 24, 26-27 and 30-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Grigoriev et al. (PNAS 1993).

Grigoriev et al. teaches a method for inhibiting gene expression by site-specifically modifying DNA using a psoralen-oligonucleotide conjugate. The method requires that the oligonucleotide component of the conjugate binds DNA site-specifically and that the psoralen component modify the DNA by intercalating and cross-linking it. Psoralen is not a nucleic acid binding enzyme.

Claim 1 is amended to recite that the nucleic acid binding agent is a nucleic acid binding enzyme. New claims 129 and 130 recite a similar limitation. Support for this limitation can be found in the specification at least on page 18 line 16. Accordingly amended claim 1 (and its dependents) and new claims 129 and 130 recite methods in which target polymers are analyzed using conjugates comprising a nucleic acid binding enzyme. The instantly claimed conjugate and methods are different from the psoralen-oligonucleotide conjugate and method taught by Grigoriev et al. at least because psoralen is not a nucleic acid binding enzyme. Claim 1 and its dependents and new claims 129 and 130 are not anticipated by Grigoriev et al.

In view of the foregoing, reconsideration and withdrawal of the rejection is respectfully requested.

*Magda et al. (US Patent No. 5,798, 491)*

Claims 1, 3-9, 16-18, 24 and 26-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Magda et al. (US Patent No. 5,798, 491).

Magda et al. teaches a method for hydrolysis and photocleavage of DNA and RNA using a texaphyrin-oligonucleotide conjugate. Texaphyrin is provided as a metal complex that hydrolyzes and photocleaves RNA and DNA. Texaphyrin is not a nucleic acid binding enzyme. Moreover the method of Magda et al. requires cleavage of the target DNA or RNA, as the method is intended to degrade particular nucleic acids. The method is not used to analyze a binding pattern of conjugates to a target polymer.

Claim 1 is amended to recite that the nucleic acid binding agent is a nucleic acid binding enzyme. New claims 129 and 130 recite a similar limitation. Support for this limitation can be

found in the specification at least on page 18 line 16. Accordingly amended claim 1 (and its dependents) and new claims 129 and 130 recite methods in which target polymers are analyzed using conjugates comprising a nucleic acid binding enzyme. The instantly claimed conjugate and methods are different from the texaphyrin-oligonucleotide conjugate and method taught by Magda et al. at least because texaphyrin is not a nucleic acid binding enzyme and the method of Magda et al. does not determine a pattern of binding of the conjugate. Claim 1 and its dependents and new claims 129 and 130 are not anticipated by Magda et al.

In view of the foregoing, reconsideration and withdrawal of the rejection is respectfully requested.

*Hyldig-Nielsen et al. (US Patent No. 6,280,946)*

Claims 1-11, 13-15, 18, 21-27, 30-32, 91 and 126-128 are rejected under 35 U.S.C. 102(b) and 102(e) as anticipated by Hyldig-Nielsen et al. (US Patent No. 6,280,946).

Hyldig-Nielsen et al. teaches a method for the detection of bacteria and/or eucarya in a sample through the use of a PNA probe that may further comprise one or more types of detectable labels, including fluorophores and enzymes. Hyldig-Neilson et al. uses the enzyme as a label from which the conjugate and its binding to a nucleic acid can be visualized. An example of a enzyme label provided by Hyldig-Neilson et al. is soy bean peroxidase which is visualized by its catalytic activity. Another example of an enzyme label provided by Hyldig-Neilson et al. is a polymerase. Hyldig-Neilson et al. however does not teach how a DNA polymerase is to be used as a label, thereby raising doubt as to whether this embodiment is even enabled. It is possible that one of ordinary skill in the art might contemplate that the polymerase is visualized via its catalytic activity (e.g., via the synthesis of a nucleic acid). The method of Hyldig-Neilson et al. also does not require the enzyme to bind to the target polymer. Instead it would appear that any such interaction could be detrimental to the ability to detect the polymerase label. The reference also does not require the enzyme to translocate along the polymer, as recited in claim 126.

Claims 1, 91 and 126 are amended to recite that the nucleic acid binding agent is a nucleic acid binding enzyme that is not detected based on its catalytic activity. New claim 129 recites a similar limitation. Support for this limitation can be found in the specification at least

on page 21 line 5-9. New claim 130 recites that the nucleic acid tag molecule is detected but the nucleic acid binding enzyme is not. Support for this limitation can be found in the specification at least on page 27 line 17. The instantly claimed methods are therefore different from the method taught by Hyldig-Neilson et al. at least because the method of Hyldig-Neilson requires detection of the polymerase within the conjugate. The rejected claims and the new claims are therefore not anticipated by Hyldig-Neilson et al.

In view of the foregoing, reconsideration and withdrawal of the rejection is respectfully requested.

*Fisher et al. (US Patent 6,362,328)*

Claims 1-8, 10-12, 18, 24-28, 30-31, 91 and 125-128 are rejected under 35 U.S.C. 102(b) as anticipated by Fisher et al. (US Patent 6,362,328).

Fisher et al. teaches a method for detecting nucleic acids using a conjugate of a nucleic acid and either S1 or P1 nuclease. The method uses the S1 or P1 nucleases as enzyme labels and requires the catalytic activity of these nucleases in order to hydrolyze a synthetic analog of FAD. The result is an enzyme amplification reaction in which binding of the conjugate to a target is visualized via the catalytic activity of the enzyme.

Claims 1, 91 and 126 are amended to recite that the nucleic acid binding agent is a nucleic acid binding enzyme that is not detected based on its catalytic activity. New claim 129 recites a similar limitation. Support for this limitation can be found in the specification at least on page 21 line 5-9. New claim 130 recites that the nucleic acid tag molecule is detected but the nucleic acid binding enzyme is not. Support for this amendment can be found in the specification at least on page 27 line 17. The instantly claimed methods are therefore different from the methods taught by Fisher et al. at least because these latter methods require detection of the nuclease bound to the nucleic acid molecule via its catalytic activity.

Claim 125 is amended to delete reference to nucleic acid binding enzymes that are nucleases.

The rejected claims and the new claims are therefore not anticipated by Fisher et al.

In view of the foregoing, reconsideration and withdrawal of the rejection is respectfully requested.

***Rejection under 35 U.S.C. §103***

Claims 19, 20, 33, 34 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of Norton et al. (Bioorganic & Medicinal Chemistry, 1995), Grigoriev et al. (PNAS, 1993), Magda et al. (US Patent 5,798,491), Hyldig-Nielsen et al. (US Patent 6,280,946) or Fisher et al. (US Patent 6,362,328) in view of Tegenfeldt et al. (WO 00/09757).

Claims 1 and 68 are amended to recite that the nucleic acid binding agent is a nucleic acid binding enzyme that binds to the polymer without cleavage and that it is not detected based on its catalytic activity. New claim 129 recites a similar limitation. New claim 130 recites that the nucleic acid binding enzyme is not detected. These limitations are not taught by the primary references, as described above. Tegenfeldt et al. also does not provide these teachings. The combination of the any of the primary references with Tegenfeldt et al. therefore does not render obvious claim 1 and its dependent claims 19, 20, 33 and 34 and claim 68 as amended, and new claims 129 and 130.

In view of the foregoing, reconsideration and withdrawal of the rejection is respectfully requested.

**CONCLUSION**

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,  
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